

BS



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/844,508      | 04/27/2001  | Alan P. Wolfe        | 8325-0014           | 9058             |

20855            7590            12/03/2004  
**ROBINS & PASTERNAK**  
1731 EMBARCADERO ROAD  
SUITE 230  
PALO ALTO, CA 94303

[REDACTED] EXAMINER

AKHAVAN, RAMIN

[REDACTED] ART UNIT      [REDACTED] PAPER NUMBER

1636

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 12/01/04 10

|                        |                        |                     |
|------------------------|------------------------|---------------------|
| <b>Advisory Action</b> | <b>Application No.</b> | <b>Applicant(s)</b> |
|                        | 09/844,508             | WOLFFE ET AL.       |
|                        | <b>Examiner</b>        | <b>Art Unit</b>     |
|                        | Ramin (Ray) Akhavan    | 1636                |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a)  The period for reply expires 3 months from the mailing date of the final rejection.
- b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.  A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.  The proposed amendment(s) will not be entered because:

- (a)  they raise new issues that would require further consideration and/or search (see NOTE below);
- (b)  they raise the issue of new matter (see Note below);
- (c)  they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d)  they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

4.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.  The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.

6.  The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.  For purposes of Appeal, the proposed amendment(s) a) will not be entered or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-6, 8, 10-13, 17-33 and 43-70.

Claim(s) withdrawn from consideration: 7, 9, 14-16, 34-42, 71 and 72.

8.  The drawing correction filed on \_\_\_\_\_ is a) approved or b) disapproved by the Examiner.

9.  Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.

10.  Other: \_\_\_\_\_

Continuation Sheet:

### **ADVISORY ACTION**

The after-final amendments are not entered because the amendments raise new issues that would require further consideration/search, as further explained below. In addition, each of Applicant's arguments in regard to rejections of the claims in the preceding action will be addressed as well.

The after-final amendments are not entered. In particular, the amendments change the scope of the invention from one of a method of altering chromatin structure with a fusion protein that does not regulate transcription to a method where the chromatin is altered so as to facilitate access to cellular DNA, which necessarily includes access to regulate transcription (whether intended or not). Therefore, the claims as considered in the preceding action were directed to a distinct invention as compared to claims as currently amended.

In addition, Applicant's argument in regard to the New Matter rejection of claims 1-6, 8, 10-13, 17-33 and 43-70 is not deemed persuasive. Applicants assert that there are multiple references in the instant application that support the fusion protein of the invention modifying chromatin but not necessarily regulating transcription. (e.g. Remarks, p. 10, ¶ 4). However, the negative limitation reciting in salient part that, "the fusion molecule does not regulate transcription" distinctly directs the invention to particular fusion proteins that can never, whether indirectly or directly, regulate transcription. Such a genus claimed is not supported by the disclosure or the particular portions of the disclosure Applicant cites.

It would be evident to one of ordinary skill in the art that the fusion molecules, as indicated throughout the specification and the cited portions therein, facilitate DNA access which *may* at least indirectly lead to transcription regulation. Therefore, the New Matter rejection under 35 U.S.C. 112, first paragraph is deemed appropriate.

With respect to the Enablement rejection of claims 1-6, 8, 10-13, 17-33 and 43-70, Applicant's argument that the disclosure is enabling for *in vivo* methods is not deemed persuasive. Applicant points to a single passage as proof that the *in vivo* methods are enabled:

Targeted modification of chromatin structure, as disclosed herein, can be used in processes such as, for example, therapeutic regulation of disease-related genes, engineering of cells for manufacture of protein pharmaceuticals, pharmaceutical discovery (including target discovery, target validation and engineering of cells for high throughput screening methods) and plant agriculture. (Remarks, p. 12)

There is insufficient teaching in this limited recitation for one of skill to use the claimed invention as prescribed. For example, there are not teachings as to what compositions/steps would be required to practice the claimed invention to achieve the disparate outcomes recited in the preceding passage. (e.g. therapeutic regulation of disease-related genes or plant agriculture). This single passage does not enable one of skill to practice the invention commensurate with the full scope of the claimed invention.

In addition, three references are provided in support of Applicant's assertion that the claimed invention is enabled (Appendices A to C). In each of the references a fusion protein consisting of a DNA-binding domain and an Activation Domain is used to induce transcription. The functional domains (i.e. Activation Domains) are not shown to actually modify chromatin.

Nonetheless, Applicants suggest that because the fusion proteins shown in the references work to activate target genes then one of skill would expect fusion proteins consisting of DNA binding domains and chromatin remodeling domains would similarly work *in vivo* to remodel chromatin. (Remarks, p. 12, next to last ¶). Put another way, Applicants are suggesting that activation domains and remodeling domains are equivalents, with respect to *in vivo* applications. Such an assertion is conclusory and does not find support in the disclosure or in the references provided, because an activation domain and a remodeling domain are two biologically distinct structures with disparate functions. If one were to accept Applicant's contention, then a fusion protein consisting of a DNA domain and *any* functional domain would be enabled for *in vivo* application by Applicant's disclosure/cited art. However, because the comparison made is between two process using functionally distinct (also patentably distinct) fusion proteins, Applicant's arguments are not deemed persuasive.

With regard to the Obviousness-Type Double Patenting (ODP), Applicant does not provide any arguments as to why the rejection is improper. Applicant only indicates that because the instant application is a parent of the reference application (10/084,826), that the ODP rejection be addressed in the reference application. This is not a proper ground for traversal.

### ***Conclusion***

Amendments after-final are not entered. Applicant's arguments traversing the rejections in the preceding action are not deemed persuasive.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ray Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached between 8:30-5:00, Monday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, PhD, can be reached on 571-272-0781. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully submitted,

Ray Akhavan/AU 1636

  
GERRY LEFFERS  
PRIMARY EXAMINER